

L35 ANSWER 231 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1989:593062 HCAPLUS Full-text
 DOCUMENT NUMBER: 111:193062
 TITLE: Production of cyclosporin derivatives with
 3-fluoroalanine at the 8-position
 INVENTOR(S): Patchett, Arthur A.; White, Raymond F.; Goegelman,
 Robert T.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: Brit. UK Pat. Appl., 22 pp.
 CODEN: BAXXDU
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2206119	A1	19881229	GB 1988-14598	19880620
GB 2206119	B2	19901031		
EP 373260	A1	19900620	EP 1988-202845	19881212
EP 373260	B1	19940309		
R: CH, DE, FR, IT, LI, NL				
CA 1338319	A1	19960507	CA 1988-585752	19881213
JP 02184699	A2	19900719	JP 1988-315185	19881215
JP 07017677	B4	19950301		

PRIORITY APPLN. INFO.: US 1987-64674 A 19870622

AB Cyclosporin derivs. are produced by incubating Tolypocladium inflatum in a fermentation broth with 3-fluoro-D-alanine or its 2-deuterated isomer. T. inflatum was incubated 14-21 days with agitation at 27° in a culture medium which contained glucose, casein peptone, MgSO₄, KH₂PO₄, NaNO₃, KClO₃, FeSO₄, and either 3-fluoro-D-alanine or 2-deutero-3-fluoro-D-alanine. The clarified broth was extracted 3 times each with methylene chloride and acetone. The exts. were pooled and dried under vacuum. The residue was solubilized with methanol, dried with anhydrous Na₂SO₄, filtered, and taken to dryness under vacuum. The samples were submitted for HPLC anal. to determine and isolate the cyclosporin derivs.

IT 123301-36-0P 123313-99-5P

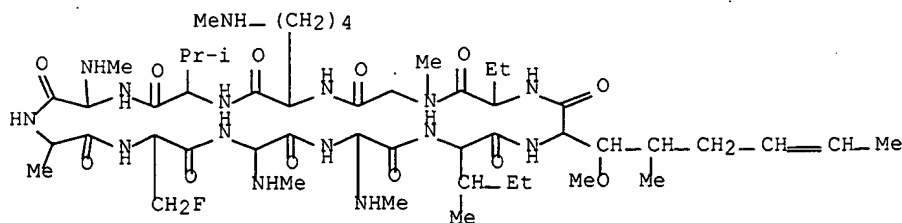
RL: IMF (Industrial manufacture); PRP (Properties); PREP

(Preparation)

(manufacture and structure of, of Tolypocladium inflatum)

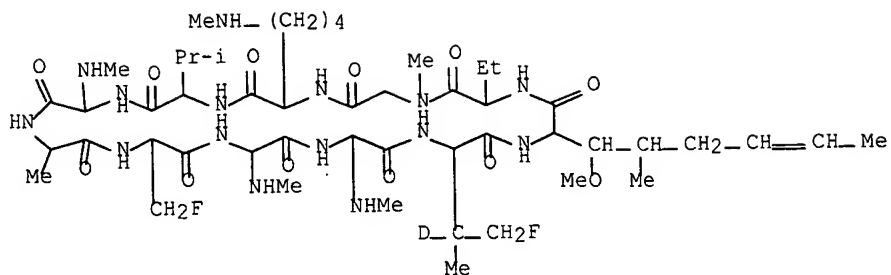
RN 123301-36-0 HCAPLUS

CN Cyclo[L-alanyl-3-fluoro-D-alanyl-L-2-(methylamino)glycyl-L-2-(methylamino)glycyl-L-isoleucyl-6,7-didehydro-3-methoxy-4-methyl-L-2-aminooctanoyl-L-2-aminobutanoyl-N-methylglycyl-N6-methyl-L-lysyl-L-valyl-L-2-(methylamino)glycyl] (9CI) (CA INDEX NAME)



RN 123313-99-5 HCAPLUS

CN Cyclo[alanyl-3-fluoroalanyl-2-(methylamino)glycyl-2-(methylamino)glycyl-4-fluoro-D-valyl-3-d-6,7-didehydro-3-methoxy-4-methyl-2-aminooctanoyl-2-aminobutanoyl-N-methylglycyl-N6-methyllysylvalyl-2-(methylamino)glycyl] (9CI) (CA INDEX NAME)



IT 59865-13-3DP, Cyclosporin A, fluoroalanine derivs.

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP

(Preparation)

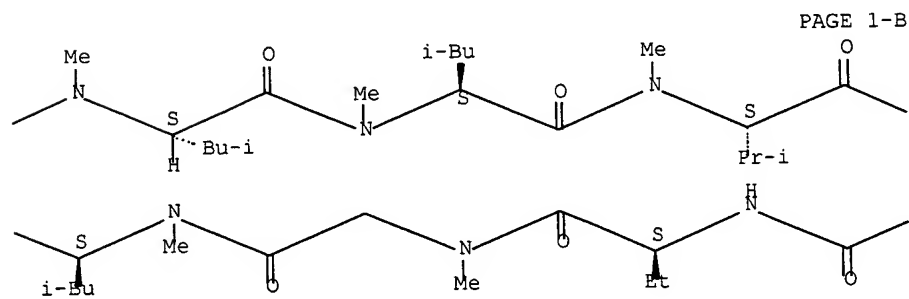
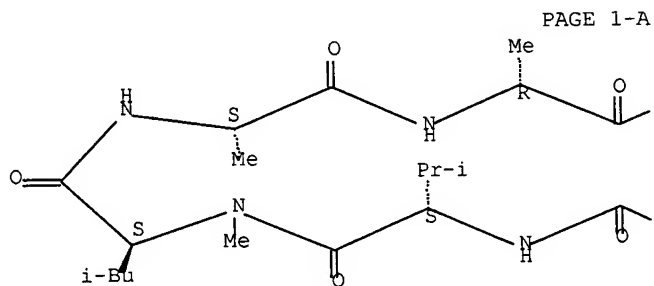
(manufacture of, with Tolypocladium inflatum)

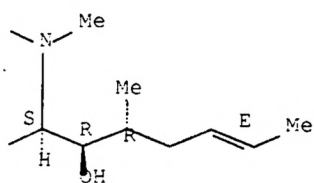
RN 59865-13-3 HCAPLUS

CN Cyclosporin A (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.





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